Listing of Claims

1. (Currently Amended) A method of creating a ~~pure~~ clinical reference solution ~~for testing multiple~~ that emulates clinically relevant sites on genes responsible for human genetic conditions, wherein the clinical reference solution is substantially free of clinically irrelevant nucleic acid ~~detrimental to the testing~~, comprising:

~~determining one or more clinically relevant sites on one or more nucleic acid sequences;~~

for each clinically relevant site, designing an arrangement of bases to emulate the clinically relevant site as isolated from ~~adjacent~~ clinically irrelevant nucleic acid that occurs adjacent to the corresponding clinically relevant site in vivo, wherein the arrangement of bases also forms ~~includes~~ one or more primer targets for differentially amplifying the clinically relevant site;

for each clinically relevant site, synthesizing[[,]] base-by-base, from end to end, a single strand of bases [[-]]~~stranded artificial version of each~~ comprising the arrangement of bases that emulates the clinically relevant site and forms the primer targets associated with ~~each~~ the clinically relevant site; and

mixing each single strand ~~artificial version of a clinically relevant site~~ into a single solution.

2. (Previously Presented) The method as recited in claim 1, wherein each clinically relevant site comprises a mutation of a normal human nucleic acid sequence, each mutation representing a human genetic condition.

3. (Canceled)

4. (Currently Amended) The method as recited in claim 1, wherein:

the synthesizing the single strand ~~one or more primer targets~~ includes ~~attaching~~ a first sequence of nucleotides attached base-by-base to a first end of ~~each of~~ the ~~one or more synthesized~~ arrangements of bases, wherein the first sequence is complementary to a nucleotide sequence of a first primer of a primer set, and

the synthesizing the single strand ~~one or more primer targets~~ includes ~~attaching~~ a second sequence of nucleotides attached base-by-base to a second end of ~~each of~~ the ~~one or more synthesized~~ arrangements of bases, wherein the second sequence is identical to a nucleotide sequence of a second primer of a primer set.

5. (Currently Amended) The method as recited in claim 1, wherein the synthesizing comprises synthesizing, base-by-base, two complementary single strands of bases, wherein:

a first strand includes ~~an artificial version of~~ one of the clinically relevant sites and a nucleic acid tag complementary to a first primer of a primer set; and

a second strand is complementary to the first strand and to a nucleic acid tag complementary to a second primer of ~~a~~ the primer set.

6-7. (Canceled)

8. (Currently Amended) The method as recited in claim 1, wherein:

each ~~of the artificial versions of a~~ clinically relevant site has an associated primer set, and wherein:

the reference solution is tuned for a specific battery of clinical tests by differentially amplifying the different clinically relevant sites to different concentrations in the reference solution.

9. (Currently Amended) The method as recited in claim 8, wherein different groups of the ~~artificial versions of the~~ clinically relevant sites in the reference solution have associated primer sets such that each different group of clinically relevant sites is amplified independently.

10. (Canceled)

11. (Previously presented) The method as recited in claim 9, wherein independently amplifying each of the groups of clinically relevant sites includes controlling a physical characteristic of the reference solution to favor an amplification capability of one primer set over an amplification capability another primer set.

12-15. (Canceled)

16. (Currently Amended) The method as recited in claim 1, further comprising adding normal human nucleic acid to the base-by-base synthesized ~~artificial versions of the~~ clinically relevant sites in order to achieve a mixture of the nucleic acids in the reference solution representing at least a segment of homologous heterozygous alleles.

17-20. (Canceled)

21. (Previously Presented) The method as recited in claim 1, further comprising joining two parts of one of the arrangements of bases together using a ligation extension to perform the synthesizing of a large arrangement of bases.

22. (Previously Presented) The method as recited in claim 21, further comprising using a bridge nucleic acid to join multiple parts of the arrangement of bases.

23. (Previously Presented) The method as recited in claim 1, further comprising using an overlap extension to join multiple parts of the arrangement of bases.

24-50. (Canceled)

51. (Withdrawn) A tagged reference nucleic acid for a polymerase chain reaction amplification, comprising:

a synthesized reference nucleic acid having a base sequence capable of being used as a reference;

a first nucleic acid tag bound to a first end of the synthesized reference nucleic acid, wherein the first nucleic acid tag has a base sequence complementary to a base sequence of a first primer of a primer set; and

a second nucleic acid tag bound to a second end of the synthesized reference nucleic acid, wherein the second nucleic acid tag has a base sequence matching a base sequence of a second primer of the primer set.

52. (Withdrawn) The tagged reference nucleic acid as recited in claim 51, wherein the synthesized reference nucleic acid includes a base sequence representing a mutation of a gene.

53. (Withdrawn) The tagged reference nucleic acid as recited in claim 52, wherein the gene comprises a cystic fibrosis transmembrane conductance regulator gene.

54-70. (Canceled)

71. (Currently Amended) A method, comprising:

designing multiple reference nucleic acids, wherein each reference nucleic acid comprises an arrangement of bases emulating a clinically relevant site of a human nucleic acid exclusive of clinically irrelevant human nucleic acid adjacent to the clinically relevant site in vivo;

synthesizing, base-by-base for each reference nucleic acid, a first mixture of various of the reference nucleic acids, wherein each of the various reference nucleic acids in the first mixture includes one or more tags allowing PCR amplification of the first mixture via a primer set specific to the tags of the first mixture; and

synthesizing, base-by-base for each reference nucleic acid, a second mixture of various of the reference nucleic acids, wherein each of the various reference nucleic acids in the second mixture includes one or more tags allowing PCR amplification of the second mixture via a second primer set specific to the tags of the second mixture.

72. (Original) The method as recited in claim 71, further comprising combining the first and second mixtures to make a single

mixture and differentially amplifying the first mixture and the second mixture in a PCR reaction by controlling amounts of the first primer set and the second primer set in the single mixture.

73. (Canceled)

74. (Currently Amended) The method as recited in claim 72 ~~73~~, further comprising adding normal human nucleic acid to the single mixture to obtain heterozygous pairs, wherein each heterozygous pair includes a normal segment of human nucleic acid and a mutated copy of the normal segment of human nucleic acid.

75. (New) The method as recited in claim 1, further comprising differentially amplifying each different single strand in the single solution to a respective clinically relevant concentration.

76. (New) The method as recited in claim 75, wherein the amplifying increases the number of each single strand exponentially.

77. (New) The method as recited in claim 75, wherein each single strand creates its own complementary single strand during the amplifying.

78. (New) A single-stranded nucleic acid reference fragment that mimics a genomic reference sample.

79. (New) The single-stranded nucleic acid of claim 78, wherein the single-stranded nucleic acid reference fragment is capable of being differentially amplified to a concentration suitable for use as a clinical reference.

80. (New) The single-stranded nucleic acid of claim 78, wherein the single-stranded nucleic acid reference fragment creates its own complementary single strand during the amplifying.